Week 9

**Opportunistic Fungi:** Do not generally cause disease unless: Tcell mediated deficiency or PMN mediated deficiency

1. **Candida:** albicans is the most common species… pseudohyphae, germ tubes, phenotype switching. Normal gut pathogen that penetrates the wall into the blood (or from a catheter). **SX** skin/soft tissue infections, mucosal, blood (maybe endocarditis/cns…). Skin and mucosal infections = t-cell mediated deficiency or diabetes. Deep infections are the result of neutropenia (tcells attack hyphae while the neutrophils attack the yeast). AIDS PT have esophagitis that is diagnostic of the first stages of AIDS (result of Th1 release of epidermal growth factors). Skin folds and wet areas are also targeted spots for satellite lesions. Vaginitis with cottage dchesse-like discharge; dissemination to the eye and vitreous fluid. **Diagnostic** basic growth on sabouraud agar (high glucose media) with yeast and psuedohypha or chlamydospores. A special test has Germ tubes develop after 2-3 hrs in serum. KOH mount is used. **Virulence due to morphologic and phenotype switching. Treat with Fluconazole but resistance increasing.**
   * **Chronic mucocutaneous candidiasis:**  rare since this grows on dry skin and the nails. It has MASSES of Ab and is the result of Tcell/zinc deficiency and endocrinopathies.

**Zygomycetes**: rapid growing, ubiquitous molds that behave like aspergillosis; anamorphs have sporangia and sporangiospores. Have hypae with mycelium bags. These hyphae are wide, irregular, lack septa and are angiotropic. Rare infections that are usually fatal. **SX** skin (see the sub Q section), GI, CNS, lungs, and possible dissemination. Can coinfect with aspergilluss. **Diagnostic** wide, aseptate, irregular hyphae. **Treat: Amp B (generally azole resistant)**

* + **Rhinocerebral zygomycosis:** nasl turbinate infection with damage around the orbit leading to black necrotic discharge from sinus/palate. DIABETES ketoacidosis is the predisposing factor
  + **Mucormycosis:** rarer than aspergillosis with macrophages better able to control. Lung infection but invasion can enter through other routes like the gut or a wound. NEUTROPENIA is the predisposing factor.

1. **Microsporidium**: unusual opportunist found AIDS PT. Very tiny spores reside within cells. Has a chitin spore wall. TEM shows a coiled polar tube, exo/edospore layer, posterior vacuole. **SX** Can cause sever GI and ocular infections most commonly (sometimes bronchial). **Diagnostic** Modified AF stain, calcofluor white stain of brochial lavage, intestinal samples **Treat: Albendazole**
2. **Pneumocystis (jirovecii):** sexual and asexual repro with human infection having free trophic form and the sporocyst/cyst. **SX** pneumonia primary or reactivation (some spread to LN, spleen, BM, Liver, GI/GU. VERY slow with shortness of breath, fever, dry cough, CXR with diffuse infiltrates. **Diagnostic** Giemsa (trophic) GMS (cyst) immune (both) or Silver stain. **Treat: Bactrim (TMP-SMX) or a pentamidine if allergy.**
3. **Cryptococcus:** saprobic/parasitic phase are present but highly overlapped. Encapsulated (mucin and melanin) with budding yeast. Worldwide in the soil (PIGEONS, Vancouver, eucalyptus tree). Blood/lymph dissemination. **SX** #1 CNS infection in untreated AIDS. Meningitis (classic symptoms in addition to fever +/-, confusion and impairment of sight). Can also cause pulmonary with nodular infiltrates, CNS parenchyma (cryptococcoma is rare and in immune competent hosts), skin/ocular/osseous dissemination. **Diagnostic** GMS or india ink of blood/CSF, antigen assay for polysaccharide capsule. **Treat: Amp B with flucytosine for 2wks then 8wks of fluconazole. Maybe a LP to relieve pressure.**
4. **Aspergillosis:** grow branched, regular, spectate hyphae with conidial heads when exposed to the air (rarely see the conidial heads in culture). Ubiquitous in the soil/decomposing matter and contracted by inhalation or transdermal from contact. Typically… killed by macro and neutron but if either missing it’s a prob. They have vascular invasion with thrombosis and proteases (the invasion is not in the blood just around the vessels). **SX** allergic RX (bronchopulmonary or sinusitis), colonization forming bronchial plugs or fungal balls in compromised pulmonary systems. Plugs aren’t in need of treatment but the balls may require surgery (grow in cavities left post Tb). **Diagnostic** PAS, Silver, GMS show tree like branches at 45 degree angles and never isolated from the blood.
   * **Necrotizing pseudomembranous bronchial aspergillus:** invasive form that is chronic and locally destructive. Seen in severe ICH with fever, infiltrates, hemoptysis/chest pain and HIGH mortality of 70%. Dissemination into blod to brain/heart/kidney/liver/spleen/GI. **Diagnostic**  Isolate from a normally sterile site perform an immune assay of galactomannan Ag in serum. **Treat: Amp B and Vericonazole.**

**Systemic Endemic infections (Primary Mycoses):** restricted to geographic niches, cause new infections and reactivation and ALL are dimorphic fungi. Coccidioidomycosis, histoplasmosis, bastomycosis, paracoccidioidomycosis and rarely penicilliosis.

1. **Blastomycosis:** Ohio River valleys. Infection occurs by inhalation/inoculation. Infiltrate macrophages with granuloma formation. Macro have some fungicidal and neutrophils use their oxidative killing. **SX** 50% asymptomatic, acute or chronic pulmonary with some extrapulmonary (skin and bone infection and maybe prostate, liver/spleen/kidney, CNS). **Diagnostic** sputum/tissue for microscopy of broad based budding yeast with conversion from mold at 37C; ELISA, complement fixation and immunodiffusion; blastomycin antigen testing. **Treat: Amp B, Itraconazole (fluconazole) surgery.**
2. **Histoplasmosis:** soil from Bat/Bird habitat (caves/farms/attics) mostly in Ohio/KY/Mississipi. Inhilation/inoculation with ingestion by alveolar macrophages and dissemination by RES or blood. **SX** 95% asymptomatic while others go from mild to severe to chronic cavitary. Disseminates to the LN and can cause mucocutaneous infections (mostly ICH, elderly, children under 2). **Diagnostic** narrow based intracellular yeast with conversion from mold at 37C. Serology and antigen testing and histoplasmin antigen at the skin (little diagnostic value). **Treat: Itraconazole, Amp B and maybe Fluconazole for CNS infections.**
   1. **African Histoplasmosis:** Larger, thick walled yeast with pronounced giant cell formation resulting in increased Skin/Bone infection.
3. **Coccidioidomycosis (immitis):** Southwest USA and Northern Mexico since it likes dry climates. **SX** primary are mostly asymptomatic though can cause fever, chest pain, cough and weight loss. Secondary (5 **%** after 6wks) causes nodular/cavitary lesions that can be progressive. 1% will have a disseminated from that is chronic/fulminant in the meninges, bones/joints and soft tissues. IF it disseminates… 25% show meningitis (Total of 0.25% have the meningitis). **Diagnostic** spherules with endospores in the sputum/tissue. 25C has arthroconidia that are barrel shaped. Complement fixation is excellent especially for prognosis and Immunodiffusion/latex agglutination are good for detection. **Treat: symptomatic, Amp B, Itro/Fluconazole.**
4. **Paracoccidioidomycosis:** Central/South America caused by inhalation. **SX** asymptomatic/latent/symptomatic (nodular lesions and rarely dissemination). **Diagnostic** samples for budding yeast with narrow base **Treat: Itraconazole and Amp B (maybe fluconazole or sulfonamides).**
5. **Penicilliosis:** SE Asia especially in HIV patients. **SX** pulmonary or disseminated **Diagnostic** HPE and culture only. **Treat: Amp B and itraconazole.**

**Subcutaneous:** confined to the dermis/subQ/adjacent tissue without systemic spread. Can be insidious or chronic with most infections starting with trauma followed by inoculation with soil/plants.

1. **Sporotrichiosis:** Sporothrix schenckii in the soil has septate hyphae with oval conidia as well as round/cigar shaped yeast. **SX** usually a skin infection that can progress to a lymphatic vessel/LN infection. RARELY can travel to joints/bones, meninges or lungs. **Diagnostic** fluid aspirate/pus/tissue with HPE (rarely see yeast) then culture to confirm mold->yeast. Can do an intradermal test for sporotrichin. **Treat: Itraconazole and potassium idodide for sub Q and AmpB itraconazole for extracutaneous.**
2. **Chromoblastomycosis:** pigmented fungi in the soil/plants **SX** verrucoid, ulcerated, crusted lesions that are flat or raised. Satellite lesions from auto-inoculation or lymphatic dissemination. Extensive keloid (scarring) that are cauliflower-like. **Diagnostic** Direct microscopy with KOH looking for colorful “sclerotic bodies”. **Treat: Surgery, Itraconazole and terbinafinez.**
3. **Eumycotic mycetoma:** Saprophytic fungi (eumycetoma) and Actinomyces “bacteria” typically in tropical climates with low rainfall. **SX** Feet, lower extremities, hands with abscesses containing granules. Can also involve local muscle and bone. **Diagnostic** tissue biopsy with demonstration of granules and distinct colony morphology. **Treat: surgery and Amp B/azoles**
4. **Subcutaneous Zymgomycosis**: saprophytes (leaf/plant debris) are implanted in the skin causing large painless masses that need biopsy for diagnosis. **Treat: Itraconazole or Potassium iodide like sporotriciosis.**
5. **Subcutaneous Phaeohyphomycosis:** Diverse, black mold growing in soil/vegetation. Causes slow growing/painless cysts that require biopsy/culture and surgical excision.

**Cutaneous**

1. **Dermatophytosis:** Trichophyton, Microsporum, Epidermophyton. They are divided based on their microscopic structure, degree of adaptation and ability to invade hair. **Trichophyton (human inf)** have numerous elliptical microconidia along the hyphae (clusters or singly). **Microsporum (animals/soil)** few elliptical microconidia borne singly along the hyphae but have thick macroconidia with 3-7 cells. Marked inflammatory respsonse as opposed to mild chronic. **Epidermophyton (human inf)** have no micro and thin smooth macro of 2-4 cells in length that occur singly or in clusters. **Treat with terbinafine, itra/fluconazole.**
   1. **Tinea barbae** beard, patches of scaly/lusterless hair and somefolliculitis (Tverucosum [rat tail], T.mentagrophytes). Azole, allylamine (these creams best), Tolnaftate, Pyridone
   2. **T.capitis** scalp and head (hair ringworm), Ectothrix (M.canis), Endothrix (T.tonsurans [chlamydoconidia), no hair parasitism (E.floccosum [clubshaped]). Grey, black, kerion, favus… (audouinii [intercalary chlamydoconidia], canis[dog snout], ferrugineum all fluoresce)
   3. **T.corporis** glabrous skin, world wide, direct contact (T.rubrum [red robins on a wire], T.mentagrophytes, E.floccosum); scattered follicular or doughnut shaped lesions. Terbinafine and maybe Itra/Fluconazole
   4. **T.cruris** groin (jock itch) with beefy red serpiginous scaly lesions. (T.rubrum, T.mentagrophytes, E.floccosum)
   5. **T.favus** mostly scalp/hair but could do skin/nails. Rare and very destructive (T.schoenleinii [antlers], M.gypseum)
   6. **T.pedis** plantar surface and feet (athletes foot) and is Moccasin, interdigital or vesicular of which the vesicular is the worst. Look to T. mentagrophytes or the other classics
   7. **T.unguium** nails (distal, proximal, white superficial, candida oncho). Distal is due to hyponichium infasion with thick/crumbly/yellow nails. Proximal in immunodeficient (T.rubrum). Superficial with soft dry nail (T.mentagrophytes)
2. **Fusarium:** yellow, pink, purple or white, red, violet colony that is very difficult to treat, causes cellulitis and has a high mortality rate. [banana boats macro]
3. **Scopularis:** conidia chains and a podery cinnamon colony
4. **Piedra (white and black)**
5. **Pityriasis versicolor:**  common scaling dermatosis with small scaly patches on the trunk and shoulders. Lesions are hypo/hyperpigmented and a micro shows “spaghetti and meatballs”. It is lipophilic and commonly caused by Malassezia fufur